## **Series: Molecular Medicine Institutions**

## The Department of Biochemistry at the University of Dundee

Philip Cohen, Ph.D., Royal Society Research Professor and Director of the Medical Research Council Protein Phosphorylation Unit and Director of the Wellcome Trust Building

In 1971 I was a postdoctoral fellow in Seattle working with Edmond Fischer at the University of Washington and looking for a suitable position back in the U.K. By July, I had received a couple of offers and been invited to attend several interviews, and so I set off for Britain thinking that I would probably accept a Lectureship (the equivalent to an Assistant Professor in the U.S.A.) at the University of Birmingham or take up a further postdoctoral fellowship at the MRC Laboratory of Molecular Biology at Cambridge. It therefore came as a surprise to my wife, Tricia, when I called at the end of the trip to suggest that we should go to the University of Dundee in Scotland instead. I explained that a new Medical Sciences Institute had just opened and that more laboratory space was available than in the other centers I had visited. I had also been most impressed with Peter Garland, the young and dynamic leader of the Department who had been appointed to the first Chair of Biochemistry in 1970. Moreover, Dundee resembled Seattle in being located in an area of outstanding natural beauty close to the sea and to mountains, attractions to which we had become accustomed. We therefore decided to take the plunge and go to Dundee, not realizing at the time the financial risk we were taking.

Scotland has a long tradition in higher education and science. The Universities of St. Andrews, Glasgow, Aberdeen, and Edinburgh were

Address correspondence and reprint requests to: Dr. Philip Cohen, Department of Biochemistry, Medical Sciences Institute, University of Dundee, Dundee, DD1 4HN, Scotland, U.K., Tel: 44 1382 344238; Fax: 44 1382 223778; E-mail: p.cohen@BAD.dundee.ac.uk

founded in 1411, 1451, 1495, and 1583, respectively, so that four Universities were already present at a time when England had only two (Cambridge and Oxford). The Royal Society of Edinburgh, established in 1783 for the "Advancement of Learning and Useful Knowledge," is one of the oldest scientific societies in the world and 21 Scots have received Nobel Prizes for medicine, physics, or chemistry in the 20th Century. By contrast, Dundee (Scotland's fourth largest city - population 170,000) was a late starter. The University College of Dundee opened in 1881, soon afterwards becoming a part of the University of St. Andrews (Fig. 1). In 1954 it was renamed Queen's College Dundee and became an independent University only in 1967.

Biochemistry at Dundee began within the Department of Physiology and its development owes much to the doggedness of Robert Cook, an Australian who had worked at Cambridge under Frederick Gowland Hopkins (the co-discoverer of vitamins). "Cookie" was appointed to a lectureship in Physiological Chemistry in 1940, and almost immediately began a campaign to make "Biochemistry" a separate Department. He was so persistent that, in order to get some peace, George Bell (the Head of Physiology and Biochemistry, as it had then become), allowed him to equip as a Biochemistry Laboratory a small building on the edge of the Campus that had previously stabled the horses used in funeral processions!

Cooke was a world authority on cholesterol. In a famous experiment he ate a 16-egg omelet and, by taking blood samples before and afterwards, demonstrated that the level of cholesterol

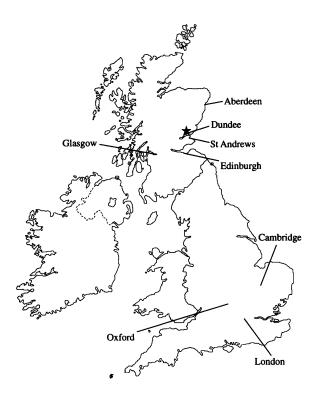


Fig. 1. Locations of Scotland's and England's oldest universities.

in the circulation did not change at all. This showed that cholesterol in the diet does not contribute significantly to the circulating level of this lipid.

Cooke realized that more expertise in different branches of the subject was necessary if biochemistry was ever to become (and expand as) a department in its own right. In 1954 he made a key appointment in recruiting Geoffrey Dutton from the University of Edinburgh who, a few years earlier, had identified UDP-glucuronic acid and its key role in drug metabolism. Dutton made Dundee a world center in glucuronidation studies, a position it still holds under Brian Burchell (his former student) in the Medical School (1). Together, Cookie and Dutton started to put Biochemistry on the map and in 1965 Cookie finally succeeded in having the Biochemistry Laboratory recognized as a separate department (a name that had previously existed only on his notepaper!). However, space was still so limited that Geoffrey Dutton was forced to "board out" his graduate students with collaborators overseas. Fortunately, the Medical Sciences Institute was built to deal with expansion of the Medical School intake that had followed Dundee's separation from St. Andrews. Biochemistry managed to grab the lion's share of the research space, and the Department moved there in 1970 when Peter Garland was appointed as its first Professor. Cookie gained a Personal Chair in 1972 and retired a year or two later.

Peter Garland came to Dundee from Bristol which, under the Chairmanship of Philip Randle, had become the premier department of biochemistry in Britain. Many had warned Peter that he was putting his career at risk by moving to an apparently remote backwater like Dundee, but he had realized that with a new building and positions to fill, plus an enthusiastic staff and an outstanding biochemist (Geoffrey Dutton) already in post, there was an opportunity to build something special. The Medical Faculty had taken the lead in providing for the first Chair of Biochemistry by making other Departments forego increases in their budgets. They were therefore somewhat miffed by Peter Garland's first decision, namely to make Biochemistry join the Faculty of Science. Although trained in medicine, Peter Garland was not convinced that the Medical Faculty would continue to be sufficiently supportive of basic research and thought it best to get a foot in both camps. A second key decision was to make the development of protein chemistry a priority and this led to my appointment as a Lecturer in late 1971 at the tender age of 26! A third important move was to allow young Staff, like myself, to concentrate on building up their research programs by giving them light teaching loads, a radical departure from normal practice in British Universities.

Having been trained at a relatively well-endowed institution (University College London), it had never occurred to me that the University of Dundee itself had little money to fund my research. In those days Britain operated a "Dual Support" system, in which the Universities were supposed to provide the infrastructure, equipment, and most of the costs of research, and one only applied to the Medical and Science Research Councils (equivalent to the National Institutes of Health and the National Science Foundation in the U.S.A.) for occasional salaries and/or particularly expensive consumables. It was clear that we would have to obtain much more money from the Research Councils and other sources than was normal at the time, but it was not easy for a junior Staff member to raise the sums needed to mount a significant research program. Despite Peter Garland giving me money from his own research grants from time to time to keep me going, matters reached a crisis point and it

was only the receipt of a special grant of £1000 from the Wellcome Trust (backed by a letter of support from Philip Randle) that allowed my laboratory to keep going through the summer of 1976. Peter Garland decided that if we stopped doing experiments because we had no money then we really were finished, and so the Department ran up a huge debt. This policy only "worked" for a time because the University finance office did not quite realize what was happening!

Fortunately, everything started to improve in the late 1970's. Grant support increased rapidly, Geoffrey Dutton received a Personal Chair and a new Principal (equivalent to the Vice Chancellor of an English University and President of an American University), Adam Neville, was appointed in 1978, who realized the importance of the Biochemistry Department for the future of all research at Dundee. The financial problems were solved by diverting money from less "productive" departments and Biochemistry was provided with more space at the expense of the Department of Anatomy with whom we shared the building. The era of molecular biology had dawned and Peter Garland realized the importance of making appointments in this area. We were fortunate to recruit Chris Higgins (who was completing a postdoctoral fellowship with Giovanna Ames at Berkeley) and David Lilley (from the Searle Pharmaceutical Company). When Peter Garland left Dundee in 1984, Graham Warren came from EMBL to replace him, and a division of Molecular Cell Biology was created with the appointment of Colin Watts and others, while the recruitment of Mike Ferguson and Steve Homans in 1987 introduced important new strengths in molecular parasitology, complex glycoconjugates, and structural biology. Many of the Staff were awarded research fellowships from organizations outside the University, which freed up money to make further appointments. It was most unusual in the 1980's for a British University Department to have so many of its Staff on "soft money" but this was crucial to its development at a time when money from the Government was diminishing all the time. In 1989 the Cancer Research Campaign agreed to set up three new research groups under the direction of David Glover, Birgit Lane, and David Lane and, when Peter Downes (a leader in the field of inositol lipid signalling) was recruited from SmithKline Beecham in the same year and the Medical Research Council decided the following year to set up the Protein Phosphorylation Unit, it was clear that the Department had arrived in a big way.

During the 1990's the Department has continued to go from strength to strength under the Chairmanship of first David Boxer and then Peter Downes. It is now a far cry from the situation of 20 years ago when I nearly had to close down my lab for the lack of £1000. The per capita research income of the Department is almost the highest in the U.K. and it has received the top ranking of 5 (now 5\*) ever since the research rating system was introduced by the Government in 1986. According to a recent survey by the Institute for Scientific Information in Philadelphia (2), University of Dundee scientists were more often cited in the areas of Biochemistry, Biology, and Molecular Biology than scientists in any of the other 100 universities in the U.K. (for papers published between 1991 and 1995 and cited over the same period). Two members of the Department have been elected Fellows of the Royal Society of London, 14 are Fellows of the Royal Society of Edinburgh, while eight have been elected members of the European Molecular Biology Organization; three honorary degrees have been awarded from U.K. and European Universities. Eight scientists who have worked in the Department have received the Colworth Medal of the British Biochemical Society (five are still at Dundee), and two others have been awarded the Fleming Medal of the British Microbiological Society. The medals are awarded annually for outstanding work carried out by investigators under the age of 36. David Lane has received a host of major international prizes for his discovery of the tumor suppressor protein p53 and is to receive the 1998 Paul Ehrlich Prize. Other recent awards include the 1996 Prelog Gold Medal in Stereochemistry from the ETH Zurich (David Lilley) and 1997 Louis Jeantet Prize for medicine (Philip Cohen). These achievements have been made despite the considerable undergraduate teaching commitments of many staff. It was therefore gratifying that the Department also received the highest ("excellent") ranking for its teaching during the 1997 assessment of teaching quality in British Universities.

It was obvious by 1990 that any further development of the Department would be severely limited by space restrictions and that a new building was required. I discussed this problem with the Scientific Director of the Wellcome Trust, Bridget Ogilvie, when she gave the Keynote Lecture at the Department's first annual



Fig. 2. The Wellcome Trust Building housing part of the Department of Biochemistry at the University of Dundee. The rest of the department is located in the adjoining Medical Sciences Institute (far right).

symposium held at Pitlochry in the Scottish Highlands in late 1990. The following year, Bridget became the overall Director of the Trust and agreed to consider a proposal to fund a new building at Dundee. This approach eventually led the Governors of the Wellcome Trust to make a donation of £10 million towards the project in December 1994, thought to be the largest single charitable donation ever given to a Scottish Institution. A further £3.5 million was raised from other local and charitable sources, and construction was completed in October 1997.

The Wellcome Trust Building (Fig. 2) is physically connected to and fully integrated with the Medical Sciences Institute and comprises four divisions. The Divisions of Gene Expression, Molecular Cell Biology and Molecular Parasitology are affiliated with the Department of Biochemistry, while the Division of Cell and Development

Biology is affiliated with the Department of Anatomy and Physiology. Recruitment to the new building has been remarkably successful, in as much as all the 18 Principal Investigators recruited from outside Dundee have been awarded Fellowships from the Cancer Research Campaign, the Medical Research Council, the Royal Society of London, and the Wellcome Trust that will pay their salaries for 4 to 10 years after the building opens. They have also raised almost £20 million in grants to support their research over the next few years. The Principal Investigators include citizens of Germany (2), Holland (2), Ireland, Italy, Switzerland, and the U.S.A. (2), as well as Britain; 450 scientists from 28 countries are currently working the Medical Sciences Institute/Wellcome Trust Building complex. Another major development is the Division of Signal Transduction Therapy, which is under

construction in the Medical Sciences Institute with a £5 million investment from four major Pharmaceutical Companies. This Division will work in partnership with the MRC Protein Phosphorylation Unit and the Inositol Lipid Signalling Laboratory to develop specific inhibitors of kinases and phosphates with therapeutic potential for the treatment of a number of diseases.

The Department of Biochemistry has had a major influence in stimulating the development of research elsewhere in the University. In recent years, several Senior Staff have moved from Biochemistry to head up other Departments, such as Biochemical Medicine (Brian Burchell) and Neuroscience (David Nicholls) in the Medical School at Ninewells Hospital, and Anatomy and Physiology (Birgit Lane and David Glover) on the main University Campus. Outstanding Postdoctoral Fellows in the Department of Biochemistry have been appointed to tenure track positions in the Departments of Biological Sciences, Chemistry, Molecular and Cellular Pathology, and Obstetrics/Gynaecology, and in the Biomedical Research Centre at Ninewells Hospital. The strength of Biochemistry at Dundee led Roland Wolf to move his Imperial Cancer Research Fund (ICRF) Molecular Pharmacology Unit from Edinburgh to Ninewells Hospital and a second ICRF Unit in Clinical Oncology was opened this year. As a result, nearly 1500 scientists are now engaged in biomedical and life sciences research at Dundee, the highest number per capita of any city in the U.K. other than Cambridge and Oxford. Expansion looks set to continue and this area will be the biggest employer in Dundee by the millenium. Cyclacel, the first Biotechnology Company spawned from the Biochemistry Department, was set up by David Lane in 1997. It is likely to be the first of many such developments.

How did the "Dundee Phenomenon" (as it has become known) happen and in such a short space of time? The critical ingredients were undoubtedly the usual mixture of outstanding leadership, plenty of space (at least to start with), the appointment of key individuals at the right moments, hard work, good luck, and the ability to capitalize on it. An organization is only as good as its staff and we take an enormous amount of

trouble over recruitment. Over overiding concerns are to appoint scientists whose research we find the most exciting (irrespective of the area in which they are working) and who we think will be interactive colleagues, enjoyable to work with, and who are interested in continuing to build on what has been achieved. This policy has led us to make many appointments in areas that we had previously thought were becoming passé, such as prokaryotic molecular genetics (Chris Higgins), or which at the time were unfashionable, like DNA supercoiling (David Lilley), or complex glycoconjugates (Mike Ferguson). However, they later became hot topics partly (or largely) as a result of the discoveries of those we had appointed! The upshot was that the continuing diversity of the Department became even more of a strength because each area of research acted as a separate growing point, due to the quality of the individuals we had appointed. More recently, as the Department has grown much larger, we have become more concerned to make appointments that not only add something distinctive, but which maximize opportunities for interaction with other research groups. Our ability to recruit key individuals has also been helped by the attractive location of Dundee and the low cost of living in the area.

Dundee markets itself as the "City of Discovery," because the ship Discovery that carried Captain Scott to the South Pole in the famous Antarctic Expedition of 1901 was built in Dundee and is now a major tourist attraction. Shipbuilding, jam factories (marmalade is a Dundee invention), and other traditional industries have disappeared, but research in molecular medicine (and other areas) is now allowing Dundee to live up to its billing. The new Wellcome Trust Building is a tremendous challenge and opportunity. We hope that the achievement of those we have appointed will raise the quality of science to even greater heights in the future.

## References

- 1. Dutton GJ. (1997) Drug Metab. Rev. 29, 997-1024.
- 2. Science Watch (1997) 8, (January/February).